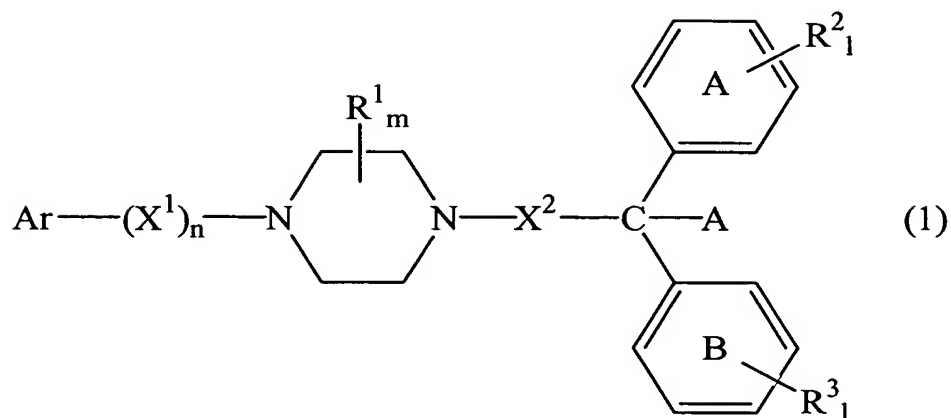


Claims

1. A compound of the formula:



wherein Ar is phenyl, a six-membered or five-membered ring which is heteroaromatic or a fused aromatic or heteroaromatic system, each of which may optionally be substituted with one or more non-interfering substituents;

X^1 is a linker containing 1-5 members;

n is 0 or 1;

each R^1 - R^3 is independently a non-interfering non-hydrogen substituent;

each l is independently 0-5;

m is 0-4;

X^2 is a linker comprising a chain of at least 5 members;

A is H, OR, SR, NR_2 , or halo wherein R is H or lower alkyl (1-6C);

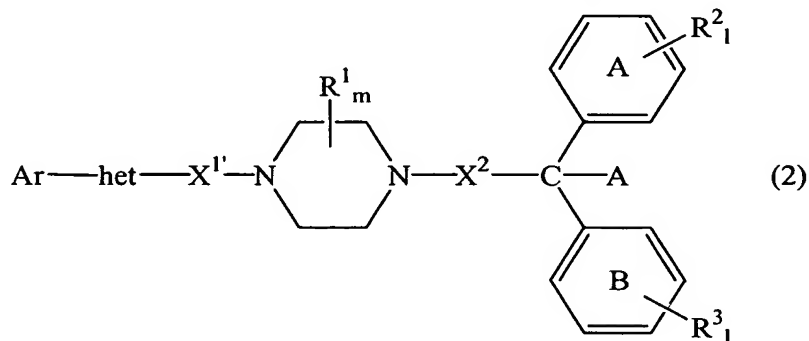
with the proviso that

- (a) Ar is a five- or six-membered heteroaryl substituent or an optionally substituted fused aromatic or heteroaromatic substituent; and/or
- (b) n is 0; and/or
- (c) m is 1-4; and/or
- (d) X^2 is alkylene substituted by =O, OR, SR, NR_2 and/or halo; and/or
- (e) X^2 is a chain of at least 6 members; and/or
- (f) X^2 contains at least one heteroatom selected from N, S and O; and/or
- (g) A is OR, SR, NR_2 or halo, wherein R is H or lower alkyl (1-6C) and/or

(h) Ar is substituted with at least one t-butyl moiety or at least one substituted alkoxy; and/or

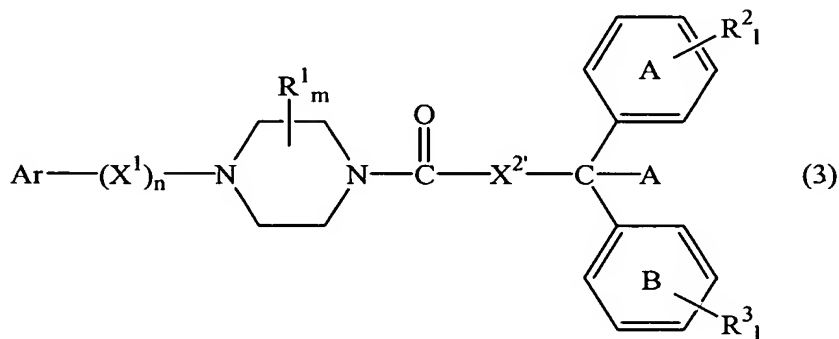
(i) X^1 includes at least one heteroatom selected from O, N and S.

2. The compound of claim 1 which is of the formula



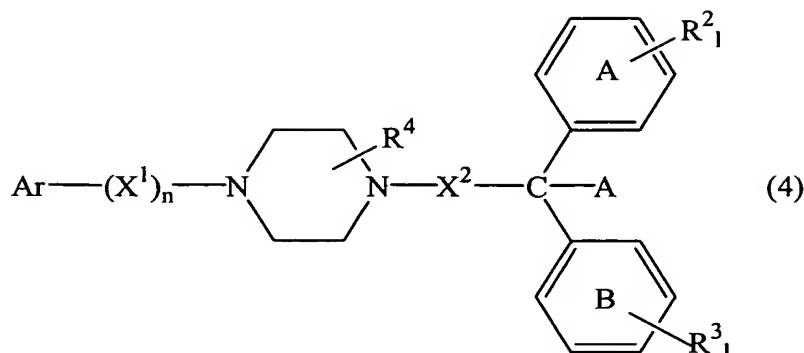
wherein Ar, R^1 - R^3 , l, m, X^2 and A are as defined above, “het” is a heteroatom selected from O, S and N, and wherein X^1 is defined as X^1 but lacking one chain member.

3. The compound of claim 1 which is of the formula



wherein Ar, X^1 , R^1 - R^3 , l, m, n, A and Ar are defined as above, and X^2 is defined as X^2 but lacking one chain member.

4. The compound of claim 1 which is of the formula



wherein R^4 is =O, or a carboxylic acid group or ester or amide thereof and Ar, R^2 - R^3 , X^1 , l, n, X^2 and A are defined as above.

5. The compound of claim 1, wherein each non-interfering substituent is independently alkyl (1-10C), alkenyl (2-10C), alkynyl (2-10C), aryl (6-10C), arylalkyl (7-16C) or arylalkenyl (7-16C) each optionally further containing 1-4 heteroatoms (N, O or S) each further optionally substituted, or is independently =O, halo, CF_3 , OCF, NO_2 , NH_2 , OH, or SH wherein S may optionally be oxidized.

6. The compound of claim 1, wherein the phenyl groups represented by A and B are linked through a bond, one or more CR_2 moieties wherein each R is H or lower alkyl (1-6C) wherein one or more of said CR_2 may be replaced by NR, O or S.

7. The compound of claim 1, wherein each l is independently 0 or 1.

8. The compound of claim 1, wherein X^2 is substituted by =O adjacent the piperazine ring.

9. The compound of claim 1, wherein X^1 is substituted by =O at the position next to the piperazine ring.

10. The compound of claim 1, wherein each of R^2 and R^3 is independently alkoxy, halo, or alkyl.

11. The compound of claim 1, wherein m is 1 and R¹ is =O or a carboxylic acid group or ester or amide thereof.
12. The compound of claim 1, wherein Ar is optionally substituted phenyl.
13. The compound of claim 12, wherein said phenyl is unsubstituted or is substituted by one or more tert-butyl, methoxy, substituted alkoxy, hydroxy and/or halo.
14. The compound of claim 13, wherein the substituted alkoxy is substituted by an amino group.
15. The compound of claim 1, wherein Ar is optionally substituted pyrimidyl, pyridyl, benzothiazole, benzimidazole or indole.
16. The compound of claim 1, which is
6,6-Bis-(4-fluoro-phenyl)-1-[4-(2-phenylsulfanyl-ethyl)-piperazin-1-yl]-hexan-1-one;
1-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-4-[2-(4-fluoro-phenoxy)-ethyl]-piperazine;
1-{4-[2-(Benzo[1,3]dioxol-5-yloxy)-ethyl]-piperazin-1-yl}-6,6-bis-(4-fluoro-phenyl)-
hexan-1-one;
1-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-4-(2-phenylsulfanyl-ethyl)-piperazine;
1-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-4-[2-(4-methoxy-phenoxy)-ethyl]-piperazine;
1-{4-[2-(2,4-Difluoro-phenoxy)-ethyl]-piperazin-1-yl}-6,6-bis-(4-fluoro-phenyl)-hexan-
1-one;
6,6-Bis-(4-fluoro-phenyl)-1-[4-(2-phenoxy-ethyl)-piperazin-1-yl]-hexan-1-one;
1-{4-[2-(2,4-Dichloro-phenoxy)-ethyl]-piperazin-1-yl}-6,6-bis-(4-fluoro-phenyl)-hexan-
1-one;
6,6-Bis-(4-fluoro-phenyl)-1-{4-[2-(4-methoxy-phenoxy)-ethyl]-piperazin-1-yl}-hexan-1-
one;
1-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-4-(2-phenoxy-ethyl)-piperazine;
6,6-Bis-(4-fluoro-phenyl)-1-{4-[2-(3,4,5-trimethoxy-phenoxy)-ethyl]-piperazin-1-yl}-
hexan-1-one;
1-{4-[2-(Benzothiazol-2-ylsulfanyl)-ethyl]-piperazin-1-yl}-6,6-bis-(4-fluoro-phenyl)-
hexan-1-one;

[4-(2-{4-[6,6-Bis-(4-fluoro-phenyl)-hexanoyl]-piperazin-1-yl}-ethoxy)-2,3,6-trimethyl-phenyl]-carbamic acid tert-butyl ester;

4-(2-{4-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-piperazin-1-yl}-ethoxy)-2,3,6-trimethyl-phenylamine;

1-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-4-[2-(2,4-dichloro-phenoxy)-ethyl]-piperazine;

[2-(4-{4-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-piperazin-1-ylmethyl}-2,6-di-tert-butyl-phenoxy)-ethyl]-dimethyl-amine;

4-{4-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-piperazin-1-ylmethyl}-2,6-di-tert-butyl-phenol;

1-[4-(3,5-Di-tert-butyl-4-methoxy-benzoyl)-piperazin-1-yl]-6,6-bis-(4-fluoro-phenyl)-hexan-1-one;

1-[4-(3,5-Di-tert-butyl-4-methoxy-benzyl)-piperazin-1-yl]-6,6-bis-(4-fluoro-phenyl)-hexan-1-one;

1-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-4-(3,5-di-tert-butyl-4-methoxy-benzyl)-piperazine;

{4-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-piperazin-1-yl}-(3,5-di-tert-butyl-4-methoxy-phenyl)-methanone;

1-{4-[3,5-Di-tert-butyl-4-(2-dimethylamino-ethoxy)-benzoyl]-piperazin-1-yl}-6,6-bis-(4-fluoro-phenyl)-hexan-1-one;

1-Benzo[1,3]dioxol-5-ylmethyl-4-[6,6-bis-(4-fluoro-phenyl)-hexyl]-piperazine;

1-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-4-(3,5-di-tert-butyl-benzyl)-piperazine;

{4-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-piperazin-1-yl}-(3,5-di-tert-butyl-4-hydroxy-phenyl)-methanone;

1-[4-(3,5-Di-tert-butyl-4-hydroxy-benzyl)-piperazin-1-yl]-6,6-bis-(4-fluoro-phenyl)-hexan-1-one;

1-[4-(3,5-Dibromo-4-hydroxy-benzoyl)-piperazin-1-yl]-6,6-bis-(4-fluoro-phenyl)-hexan-1-one;

1-[4-(3,5-Di-tert-butyl-4-hydroxy-benzoyl)-piperazin-1-yl]-6,6-bis-(4-fluoro-phenyl)-hexan-1-one;

1-[4-(3,5-Di-tert-butyl-benzoyl)-piperazin-1-yl]-6,6-bis-(4-fluoro-phenyl)-hexan-1-one;

1-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-4-(4-tert-butyl-benzyl)-piperazine;

1-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-4-(9H-thioxanthen-9-yl)-piperazine;

2-{4-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-piperazin-1-yl}-benzothiazole;

6,6-Bis-(4-fluoro-phenyl)-1-(4-pyrimidin-2-yl-piperazin-1-yl)-hexan-1-one;

2-{4-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-piperazin-1-yl}-pyrimidine;
6,6-Bis-(4-fluoro-phenyl)-1-[4-(9H-thioxanthen-9-yl)-piperazin-1-yl]-hexan-1-one;
1-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-4-(3,4,5-trimethoxy-benzyl)-piperazine-2-carboxylic acid ethyl ester;
6,6-Bis-(4-fluoro-phenyl)-1-{4-[2-(3,4,5-trimethoxy-benzylamino)-ethyl]-piperazin-1-yl}-hexan-1-one;
9,9-Bis-(4-fluoro-phenyl)-1-[4-(3,4,5-trimethoxy-benzyl)-piperazin-1-yl]-nonan-1-one;
(2-{4-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-piperazin-1-yl}-ethyl)-phenyl-amine;
1-[9,9-Bis-(4-fluoro-phenyl)-nonyl]-4-(3,4,5-trimethoxy-benzyl)-piperazine;
(4-{4-[Bis-(4-fluoro-phenyl)-methoxy]-butyl}-piperazin-1-yl)-(3,4,5-trimethoxy-phenyl)-methanone;
6,6-Bis-(4-fluoro-phenyl)-1-[4-(4-trifluoromethoxy-benzoyl)-piperazin-1-yl]-hexan-2-one;
1-[4-(4-Bromo-benzoyl)-piperazin-1-yl]-6,6-bis-(4-fluoro-phenyl)-hexan-1-one;
6,6-Bis-(4-fluoro-phenyl)-5-hydroxy-1-[4-(3,4,5-trimethoxy-benzoyl)-piperazin-1-yl]-hexan-1-one;
1-{4-[Bis-(4-fluoro-phenyl)-methoxy]-butyl}-4-(3,4,5-trimethoxy-benzyl)-piperazine;
6,6-Bis-(4-fluoro-phenyl)-6-hydroxy-1-[4-(3,4,5-trimethoxy-benzoyl)-piperazin-1-yl]-hexan-1-one;
4-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-1-(3,4,5-trimethoxy-benzyl)-piperazine-2-carboxylic acid;
4-[6,6-Bis-(4-fluoro-phenyl)-hexanoyl]-1-(3,4,5-trimethoxy-benzyl)-piperazin-2-one;
1-[6,6-Bis-(4-fluoro-phenyl)-hexanoyl]-4-(3,5-di-tert-butyl-4-methoxy-benzoyl)-piperazin-2-one;
1-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-4-(3,4,5-trimethoxy-benzoyl)-piperazin-2-one;
4-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-1-(3,4,5-trimethoxy-benzyl)-piperazin-2-one;
4-[6,6-Bis-(4-fluoro-phenyl)-hexanoyl]-1-(3,5-di-tert-butyl-4-methoxy-benzyl)-piperazin-2-one;
4-[6,6-Bis-(4-fluoro-phenyl)-hexanoyl]-1-[2-(4-fluoro-phenoxy)-ethyl]-piperazin-2-one;
1-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-4-(3,5-di-tert-butyl-4-methoxy-benzoyl)-piperazin-2-one;

4-[6,6-Bis-(4-fluoro-phenyl)-hexanoyl]-1-(3,5-di-tert-butyl-4-methoxy-benzoyl)-piperazin-2-one;

1-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-4-(3,5-di-tert-butyl-4-methoxy-benzyl)-piperazin-2-one;

1-[6,6-Bis-(4-fluoro-phenyl)-hexanoyl]-4-(3,5-di-tert-butyl-4-hydroxy-benzoyl)-piperazin-2-one;

6,6-Bis-(4-fluoro-phenyl)-1-[4-(3,4,5-trimethoxy-benzoyl)-piperazin-1-yl]-hex-5-en-1-one;

1-{4-[2-(3,4-Dimethoxy-phenoxy)-ethyl]-piperazin-1-yl}-6,6-bis-(4-fluoro-phenyl)-hexan-1-one;

1-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-4-[2-(3,4-dimethoxy-phenoxy)-ethyl]-piperazine;

1-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-4-(3,4,5-trimethoxy-benzyl)-piperazine-2-carboxylic acid;

4-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-1-(3,4,5-trimethoxy-benzyl)-piperazine-2-carboxylic acid ethyl ester;

1-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-4-(3,4-dimethoxy-benzyl)-piperazine;

1-[4-(3,4-Dimethoxy-benzoyl)-piperazin-1-yl]-6,6-bis-(4-fluoro-phenyl)-hexan-1-one;

1-[2-(Benzo[1,3]dioxol-5-yloxy)-ethyl]-4-[6,6-bis-(4-fluoro-phenyl)-hexyl]-piperazine;

1-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-4-[2-(3,4,5-trimethoxy-phenoxy)-ethyl]-piperazine;

1-(4-Amino-2,3,5-trimethyl-phenoxy)-3-{4-[6,6-bis-(4-fluoro-phenyl)-hexyl]-piperazin-1-yl}-propan-2-ol;

1-{4-[3-(4-Amino-2,3,5-trimethyl-phenoxy)-2-hydroxy-propyl]-piperazin-1-yl}-6,6-bis-(4-fluoro-phenyl)-hexan-1-one;

1-(4-Benzothiazol-2-yl)-piperazin-1-yl)-6,6-bis-(4-fluoro-phenyl)-hexan-1-one;

1-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-4-(3,5-bis-trifluoromethyl-benzyl)-piperazine;

1-[4-(3,5-Bis-trifluoromethyl-benzoyl)-piperazin-1-yl]-6,6-bis-(4-fluoro-phenyl)-hexan-1-one;

1-[4-(4-tert-Butyl-benzoyl)-piperazin-1-yl]-6,6-bis-(4-fluoro-phenyl)-hexan-1-one;

1-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-4-(4-bromo-benzyl)-piperazine;

2-(2-{4-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-piperazin-1-yl}-ethylsulfanyl)-benzothiazole;

6,6-Bis-(4-fluoro-phenyl)-1-[4-(4-hydroxy-3,5-dimethoxy-benzoyl)-piperazin-1-yl]-hexan-1-one;

4-{4-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-piperazin-1-ylmethyl}-2,6-dibromo-phenol;
1-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-4-(4-trifluoromethoxy-benzyl)-piperazine;
(2-{4-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-piperazin-1-yl}-ethyl)-(3,4,5-trimethoxy-benzyl)-amine;
1-{4-[2-(4-Fluoro-phenoxy)-ethyl]-piperazin-1-yl}-6,6-bis-(4-fluoro-phenyl)-hexan-1-one;
6,6-Bis-(4-fluoro-phenyl)-1-[4-(2-phenylamino-ethyl)-piperazin-1-yl]-hexan-1-one;
1-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-4-[2-(2,4-difluoro-phenoxy)-ethyl]-piperazine;
N-(2-{4-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-piperazin-1-yl}-2-oxo-ethyl)-benzamide;
N-(2-{4-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-piperazin-1-yl}-2-oxo-ethyl)-4-chloro-benzamide;
N-(2-{4-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-piperazin-1-yl}-2-oxo-ethyl)-4-methyl-benzamide;
N-(2-{4-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-piperazin-1-yl}-2-oxo-ethyl)-4-isopropyl-benzamide;
N-(2-{4-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-piperazin-1-yl}-2-oxo-ethyl)-4-tert-butyl-benzamide;
N-(2-{4-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-piperazin-1-yl}-2-oxo-ethyl)-4-fluoro-benzamide;
N-(2-{4-[6,6-Bis-(4-fluoro-phenyl)-hexanoyl]-piperazin-1-yl}-2-oxo-ethyl)-benzamide;
N-(2-{4-[6,6-Bis-(4-fluoro-phenyl)-hexanoyl]-piperazin-1-yl}-2-oxo-ethyl)-4-chloro-benzamide;
N-(2-{4-[6,6-Bis-(4-fluoro-phenyl)-hexanoyl]-piperazin-1-yl}-2-oxo-ethyl)-4-methyl-benzamide;
N-(2-{4-[6,6-Bis-(4-fluoro-phenyl)-hexanoyl]-piperazin-1-yl}-2-oxo-ethyl)-4-isopropyl-benzamide;
N-(2-{4-[6,6-Bis-(4-fluoro-phenyl)-hexanoyl]-piperazin-1-yl}-2-oxo-ethyl)-4-tert-butyl-benzamide;
N-(2-{4-[6,6-Bis-(4-fluoro-phenyl)-hexanoyl]-piperazin-1-yl}-2-oxo-ethyl)-4-fluoro-benzamide;
1-[4-(2-Benzylamino-ethyl)-piperazin-1-yl]-6,6-bis-(4-fluoro-phenyl)-hexan-1-one;

1-{4-[2-(4-Chloro-benzylamino)-ethyl]-piperazin-1-yl}-6,6-bis-(4-fluoro-phenyl)-hexan-1-one;

6,6-Bis-(4-fluoro-phenyl)-1-{4-[2-(4-methyl-benzylamino)-ethyl]-piperazin-1-yl}-hexan-1-one;

6,6-Bis-(4-fluoro-phenyl)-1-{4-[2-(4-isopropyl-benzylamino)-ethyl]-piperazin-1-yl}-hexan-1-one;

1-{4-[2-(4-tert-Butyl-benzylamino)-ethyl]-piperazin-1-yl}-6,6-bis-(4-fluoro-phenyl)-hexan-1-one;

1-{4-[2-(4-Fluoro-benzylamino)-ethyl]-piperazin-1-yl}-6,6-bis-(4-fluoro-phenyl)-hexan-1-one;

6,6-Bis-(4-fluoro-phenyl)-1-[4-(1-hydroxy-pyridine-4-carbonyl)-piperazin-1-yl]-hexan-1-one;

4-{4-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-piperazin-1-ylmethyl}-2,6-dimethoxy-phenol;

9,9-Diphenyl-1-[4-(3,4,5-trimethoxy-benzyl)-piperazin-1-yl]-nonan-1-one;

1-[4-(3,5-Di-tert-butyl-4-methoxy-benzoyl)-2-methyl-piperazin-1-yl]-6,6-bis-(4-fluoro-phenyl)-hexan-1-one;

1-[4-(3,5-Di-tert-butyl-4-methoxy-benzoyl)-3-methyl-piperazin-1-yl]-6,6-bis-(4-fluoro-phenyl)-hexan-1-one;

1-[4-(3,5-Di-tert-butyl-benzoyl)-2-methyl-piperazin-1-yl]-6,6-bis-(4-fluoro-phenyl)-hexan-1-one; or

1-[4-(4-tert-Butyl-benzoyl)-2-methyl-piperazin-1-yl]-6,6-bis-(4-fluoro-phenyl)-hexan-1-one.

17. A pharmaceutical composition for use in treating conditions characterized by calcium channel activity which composition comprises, in admixture with a pharmaceutically acceptable excipient, a unit dosage amount of at least one compound of claim 1.

18. A method to treat conditions associated with calcium channel activity in a subject which method comprises administering to a subject in need of such treatment at least one compound of claim 1 or a pharmaceutical composition thereof.